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EXAMINER

NIEBAUER, RONALD T

ART UNIT

PAPER NUMBER

1654

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/559,996	<b>Applicant(s)</b> KRAHMER ET AL.	
	<b>Examiner</b> RONALD T. NIEBAUER	<b>Art Unit</b> 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 15 April 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 3-12 and 15-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,13 and 14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 December 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/27/06</u> .  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election with traverse of Group I (claims 1-5,9-15,17-20) and the species where Z is formula Xc (see specification page 15) in which b is 2, c is 2, d is 3, P is H and R1 is C5 alkoxy residue; W is hydrogen; X is CH<sub>3</sub>-(O-CH<sub>2</sub>CH<sub>2</sub>)<sub>3</sub>-OH wherein X is attached through the OH group; V is tetraethylene glycol in the reply filed on 4/15/08 is acknowledged. It is noted that the replies dated 2/27/08 and 11/16/08 and 9/13/07 were not complete and are thus not relied upon.

The species has been interpreted as being of formula Ia since there is no X in formula Ib. Since the valency of oxygen would not be proper (oxygen would be bonded to a carbon, hydrogen, and nitrogen) as stated by applicant, the X has been taken to be attached via the O (not an OH) such that the oxygen is bonded to a nitrogen and carbon.

The traversal is on the ground(s) that the groups are linked by a common inventive concept, namely compounds, which are not anticipated by the prior art .

This is not found persuasive. First, it is noted that applicant has amended the claims such that the art cited in the original restriction requirement is not applicable. However, Rathore et al. (Journal of Polymer Science , Part A:Polymer Chemistry, 2000 v38(2) pages 352-366) as discussed in detail below teach compounds of the instant invention as currently interpreted. Thus, the technical feature is not a contribution over the prior art and the claims lack unity. As discussed in the restriction requirement dated 8/17/07 the invention of Group II are structurally distinct from the compounds of Group I and III.

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The requirement is still deemed proper and is therefore made FINAL.

The elected species, as currently interpreted (the species has been interpreted as being of formula Ia since there is no X in formula Ib; since the valency of oxygen would not be proper as stated by applicant, the X has been taken to be attached via the O (not an OH)), was found to be free of the prior art. In accord with section 803.02 of the MPEP the search was then extended to other species and Rathore et al. (Journal of Polymer Science , Part A:Polymer Chemistry, 2000 v38(2) pages 352-366) was found as cited below. As such, the examination has been extended to the extent necessary to determine patentability of the Markush-type claim.

Claims 3-12,15-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention/species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/15/08.

Claims 1-2,13-14 are under consideration.

### ***Specification***

The disclosure is objected to because of the following informalities:

The specification includes pages 50 and 52. However, page 51 is missing.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

#### **Arrangement of the Specification**

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without

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underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
- (d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
- (e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
- (f) BACKGROUND OF THE INVENTION.
  - (1) Field of the Invention.
  - (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (g) BRIEF SUMMARY OF THE INVENTION.
- (h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
- (i) DETAILED DESCRIPTION OF THE INVENTION.
- (j) CLAIM OR CLAIMS (commencing on a separate sheet).
- (k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
- (l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

The section heading regarding the description of the drawings (see MPEP section 608.01f), for example, has not been included in the instant invention.

Appropriate correction is required.

### ***Information Disclosure Statement***

References DE 19720165, EP 1104677, and Domling et al are cited in the IDS and are not in the English language. The references are cited in an English translation of a search report which meets the requirement of a concise explanation (see MPEP section 609.04(a) III). The references have only been considered to the extent of the description provided in the search report.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claims 1-2,13-14** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (and dependent claims 2,13-14) recite ‘a compound of the formula...’ and then recites two formulas (formula Ia and formula Ib). Since 2 different formulas do not identify a single compound the claimed invention is unclear. It is unclear if the compound comprises both of the formulas or comprises one of the formulas. Further, it is noted that the claim states that the compound is of the formula, not a compound of one of the formulas. The metes and bounds of the claim are unclear.

Claim 1 recites that particular residues ‘carries a binding group Y’. The use of the term ‘carries’ renders the term unclear. In particular it is not clear if Y is a necessary structural feature of the compound (i.e. the compound comprises Y) or if the group Y is something distinct and separate from the compound.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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**Claims 1-2,13-14** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

“To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that “the inventor invented the claimed invention.” *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (“[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.”). Thus, an applicant complies with the written description requirement “by describing the invention, with all its claimed limitations, not that which makes it obvious,” and by using “such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.” *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.” *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

“A written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as by structure, formula, [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) (“In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...”) *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is “not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.” MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include “level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient.” MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a compounds (claim 1 and dependent claims 2,13-14).



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Although unclear (see 112 2<sup>nd</sup>) for purposes of examination the claims have been interpreted such that the compound is of formula Ia OR formula Ib. Group Y has been interpreted to be a part of the claimed compound.

*(1) Level of skill and knowledge in the art:*

The level of skill in the art is high.

*(2) Partial structure:*

Claim 1 recites formula Ia and formula Ib. As currently interpreted (see 112 2<sup>nd</sup>) the claims are taken to be of formula Ia or formula Ib. In both formula Ia and Ib V,W,X, and Z can be a hydrocarbon residue which can contain heteroatoms. In considering the size of the genus, the specification (last paragraph page 12 – page 13) states that hydrocarbon residues can contain from 1 to 100000 C atoms and there can be 1 to 1000 heteroatoms. Since formula Ia, for example, contains 5 variables (V, two Ws, X, and Z) that can be hydrocarbons with heteroatoms there are up to 500000 C atoms with 5000 heteroatoms possible. Hence, there is substantial variability in the genus. As noted above, if the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus.

Although claim 1 recites formula Ib, there appear to be no examples provided of compounds of formula Ib. In particular, it is noted that formula Ib includes CW2-O-CO while the examples appear to be drawn to compounds that include CW2-NX-CO. As noted above, although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618. In the instant case, there appear to be no examples of species of formula Ib

and as such one would not recognize that the applicant was in possession of the subgenus of compounds of formula Ib.

Although claim 1 recites that any of V,W,X, and Z can exhibit a group of formula IIa, the examples appear to be drawn to compounds in which only X exhibits a group of formula IIa. As discussed above, there is substantial variability in the genus of compounds of formula Ia. The examples provided at page 36 and page 41 for example are limited to compounds in which only X exhibits a group of formula IIa and in which n is 3. Further, all the examples in which the compounds are used as conjugates are drawn to substance 16 as shown on page 41. Due to the substantial variability of the genus, substance 16 is not representative of the genus of claims 1-2,13-14.

Further, although the claims recite formulas the recited formulas are not precise so as to distinguish the subject matter from other materials (see *In re Smythe* cited above). As discussed above the claims are very general and include up to 500000 C atoms with 5000 heteroatoms. However, the claimed formulas do not precisely distinguish the instant compound from other materials. The formulas do not provide sufficient relevant identifying characteristics of the claimed invention. No significant core structure is present for the compounds of the instant invention.

*(3) Physical and/or chemical properties and (4) Functional characteristics:*

The claims recite that the compounds carry a binding group (Y) that binds to a wide variety of groups (claim 2). For example, the binding group is 'able to bond to silicon-containing surfaces' (claim 2). However, the recitation of a binding group does not provide significant

common attributes or characteristics that identify members of the claimed genus. Further, a relationship is not provided between structure and function so that the structure related to functions such as 'able to bond to silicon-containing surfaces' would be evident. Although not expressly stated in the claims, the title suggests that the compounds are for modifying biopharmaceuticals. However, there is no correlation provided between structure and the ability to effectively modify biopharmaceuticals. As such, one of ordinary skill in the art could not predict which compounds would be effective to modify biopharmaceuticals.

*(5) Method of making the claimed invention:*

The specification (specifically example 1 page 36) describes synthesis of a compound of formula Ia, however the specification fail to describe the synthesis of a representative number of compounds such as compounds of formula Ib.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1-2,13-14 is/are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are many. The specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of compounds identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the

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specification does “little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.”) Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**Claims 1-2,13-14** are rejected under 35 U.S.C. 102(b) as being anticipated by Rathore et al. (Journal of Polymer Science , Part A:Polymer Chemistry, 2000 v38(2) pages 352-366).

Rathore teach copolymers containing polyethylene glycol segments and peptide segments (abstract). In scheme 1 (page 357) Rathore teach structure 6 (Boc-GAGA-HN(CH<sub>2</sub>CH<sub>2</sub>O)5-CH<sub>2</sub>CH<sub>2</sub>NH-AGAG-Boc). It is noted that the structures of the amino acids of structure 6 are shown in chart 1 (page 353) and scheme 2 for example. Structure 6 of Rathore is:

In comparison to the instant invention, Z (A-HN(CH<sub>2</sub>CH<sub>2</sub>O)<sub>5</sub>-CH<sub>2</sub>CH<sub>2</sub>NH-AGAG-Boc) includes the second alanine side chain residue and the polyethylene portion and second peptidic portion. As such, Z (A-HN(CH<sub>2</sub>CH<sub>2</sub>O)<sub>5</sub>-CH<sub>2</sub>CH<sub>2</sub>NH-AGAG-Boc) contains a formula of formula IIa of the instant invention where R<sub>1</sub> includes the second alanine side chain; n is 5. X and W (as part of the 2nd glycine residue) are hydrogen. V (Boc-GA) includes the first glycine

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residue and the side chain of the first alanine residue (i.e. a hydrocarbon residue which can contain hydrocarbons).

Scheme 2 (page 357) shows that the NH residues, for example, can act in hydrogen bonding and as such the compound contains a binding group Y. In particular hydrogen bonding is shown with carbonyl groups (scheme 2 page 357) thus meeting the limitations recited in claim 2 of the instant invention. Taken together, the compound of Rathore meet the structural limitations of claims 1-2 of the instant invention.

Rathore teach (page 355 1<sup>st</sup> column last two paragraphs) the synthesis of structure 6 in solution so the compound is necessarily part of a composition thus meeting the structural limitations of claims 13-14 of the instant invention. It is noted that the recitation of 'diagnostic' in claim 14 does not result in a structural difference. As such Rathore meet the limitations of the claims.

Although unclear (see 112 2<sup>nd</sup>) for purposes of examination the claims have been interpreted such that the compound is of formula Ia OR formula Ib. Group Y has been interpreted to be a part of the claimed compound.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ronald T Niebauer/  
Examiner, Art Unit 1654

/Anish Gupta/  
Primary Examiner, Art Unit 1654